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SOLID-STATE CHARACTERIZATION OF THE NEW MOLECULAR SALTS OF PYRIDOXINE

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INTRODUCTION

The intermolecular motifs, mainly H-bonding between co-crystallizing Active Pharmaceutical Ingredient (API) and coformer (CF), cause the extent of charge transfer in crystal structures of molecular crystals of pharmaceutical relevance to be in range of formation neutral or ionic co-crystals to molecular salts. These molecular crystals exert physical properties (API solubility and dissolution rate) and performance (API pharmacokinetics and bioavailability) that are different in comparison with all solid forms in which API may exist.

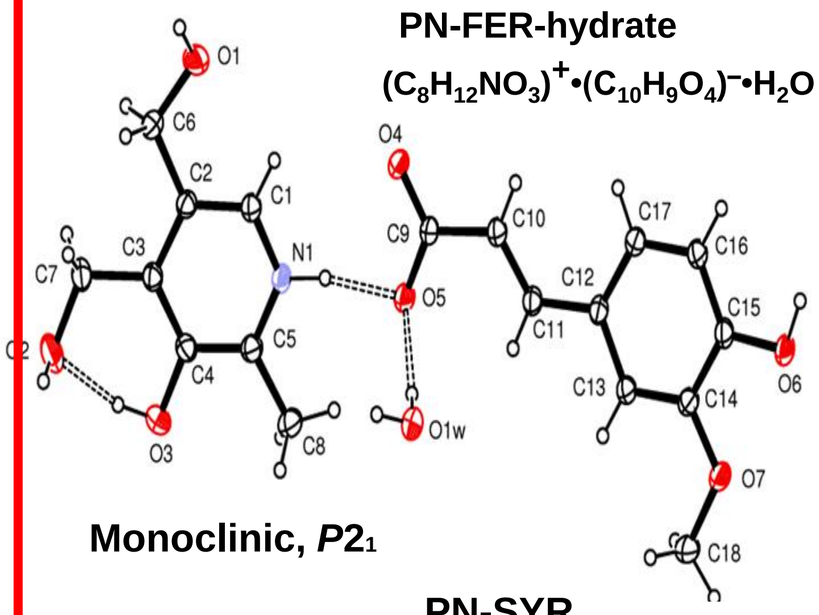
PURPOSE OF THE STUDY

To optimize the method of preparation of the two molecular salts of API pyridoxine (vitamin B6, hereforth referred as PN), the β-hydroxypyridine derivative, with two aromatic acids, ferulic acid (FER) and syringic acid (SYR), that are potent antioxidants: PN-FER-hydrate in 1:1:1 molar ratio and PN-SYR 1:1 molar ratio and to carry out their solid-state characterization.

ORTEPIII diagrams

PN-FER-hydrate

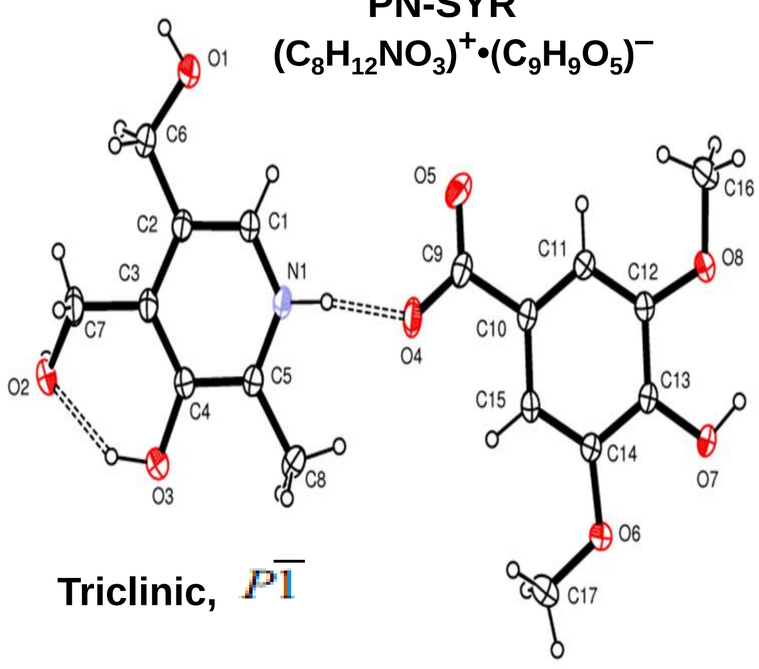
$(C_8H_{12}NO_3)^+ \bullet (C_{10}H_9O_4)^- \bullet H_2O$



Monoclinic, $P2_1$

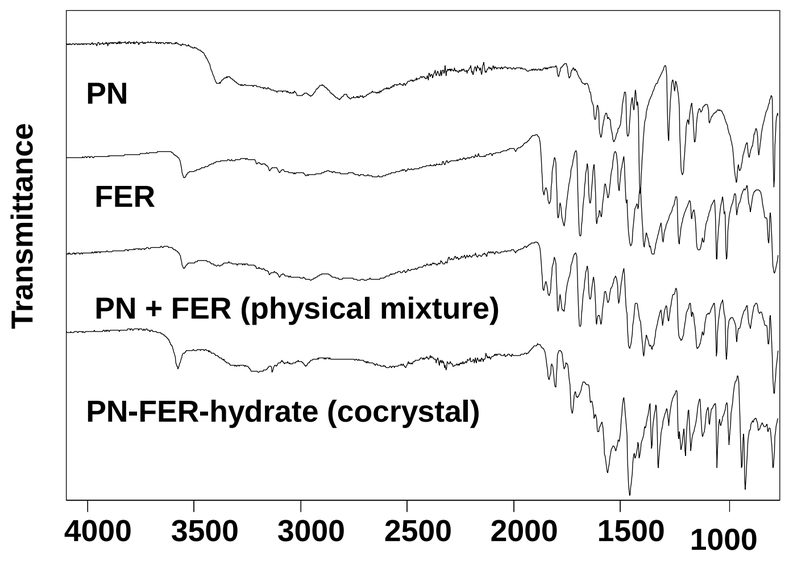
PN-SYR

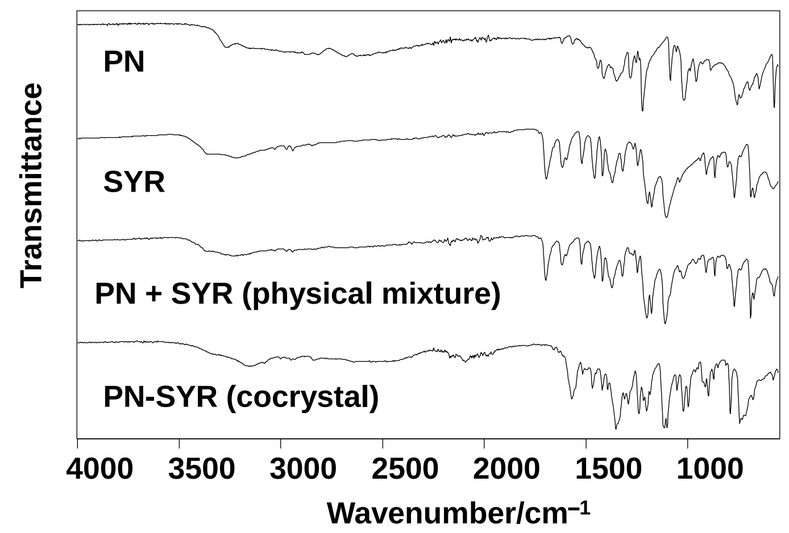
$(C_8H_{12}NO_3)^+ \bullet (C_9H_9O_5)^-$



Triclinic, $P\bar{1}$

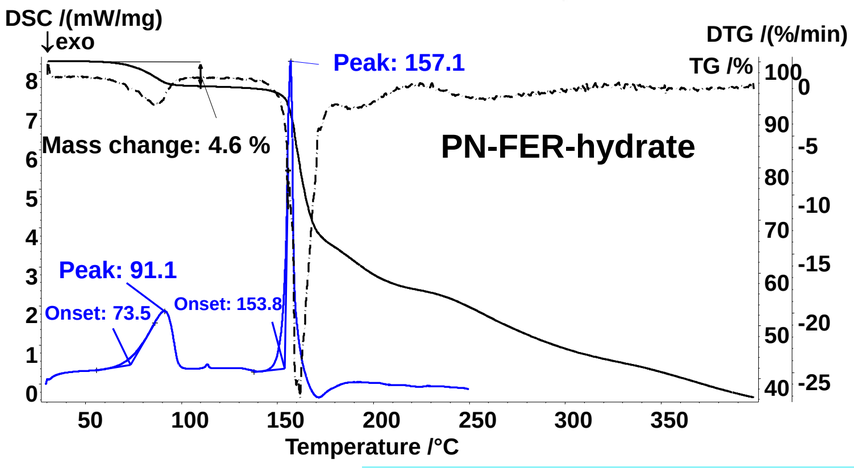
FTIR spectra – Band assignment



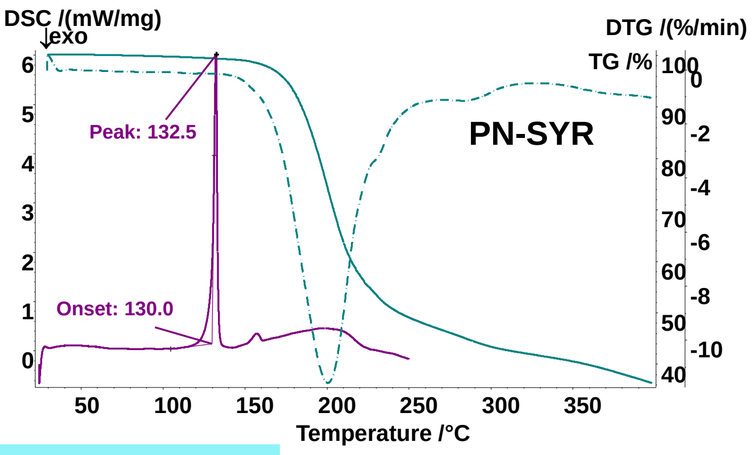


PN-FER cocrystal		PN-SYR cocrystal	
Assignment	**Pos./cm^{-1}**	**Assignment**	**Pos./cm^{-1}**
v(O–H), phenol	3459		
v(O–H), alcohol	3204	*v*(O–H), –COOH	3147
v(C–H), aromatic	3095, 3056	*v*(C–H), aromatic	3080
v_{as}(C–H), $-CH_3$	2999	v_{as}(C–H), $-CH_3$	2999, 2969
v_s(C–H), $-CH_3$	2943	v_s(C–H), $-CH_3$	2949, 2932
v(C–H), $-OCH_3$	2839	*v*(C–H), $-OCH_3$	2832
v(C=O),–COOH	1661	*v*(C=O), –COOH	1655
v(C=C), Ar-C=C	1630	*v*(C=C), aromatic	1630
v(C=N), pyridine *v*(C=C–C), aromatic ring	1553 1587,1523	*v*(C=N), pyridine *v*(C=C–C), aromatic ring	1567 1612,1524
δ(C–H), $-CH_3$	1460	*δ*(C–H), $-CH_3$	1465
δ(O–H), –COOH	1423	*δ*(C–H), $-CH_2$	1417
		δ(O–H), phenol	1390
δ(O–H), phenol	1370	*δ*(O–H), phenol	1350
v(C–O),–COOH	1338, 1321	*v*(C–O), –COOH	1307
v(C–O), Ph–OCH_3	1269	*δ*(O–H), alcohol *v*(C–O), Ar–OCH_3	1298, 1237
v(C–O), phenol	1220	*v*(C–O), phenol *v*(C–O), phenol	1214, 1199
δ(C–H), aromatic	1164	*δ*(C–H), aromatic	1181
v(C–O), alcohol	1081	*δ*(C–H), aromatic *v*(C–O), alcohol	1111, 1099
v(H_3C–OAr), alkyl *v*(C–O), alcohol	1033, 1021, 1000	*v*(H_3C–OAr), alkyl *v*(Ar–C)	1049, 1018, 995
δ(O–H), –COOH	974,	*δ*(O–H) *γ*(O–H), –COOH	953 924,
γ(C–H), aromatic	917, 884, 847, 830	*γ*(C–H), aromatic	895, 870

Thermal analysis (DSC/TG)



	T (onset)/°C	T (peak)/°C	Mass loss/%	Origin
PN-FER-hydrate	73.5	91.1	4.7 (up to 110 °C)	Water evaporation
	153.8	157.1	Significant	Melting with decomposition
PN-SYR	130	132.5	Significant	Melting with decomposition



Correlation of crystallographic parameters with FTIR and thermal properties

TYPE OF COCRYSTAL	*M/M*	C—O length (Å) (carboxylate)	C—C—O angle (°) carboxylate-aromatic ring	C1—N1—C5 bond angle (°)	N1—H...O4 length (Å)	N1—H...O4 dihedral angle (°)	FTIR spectra assignment/ Wavenumber (cm^{-1})	Malting points (DSC/TG) °C
PN-FER-hydrate	1:1:1	O4—C9 1.252(2) O5—C9 1.268(3)	O4—C9—C10 118.83 O5—C9—C10 118.69	123.26	2.641	1.3	*v*(C=O),–COOH/ 1661 *v*(C–O),–COOH/ 1338 *δ*(C–H), aromatic/ 1164 v(C=N), pyridine/ 1553	Loss of water (4.7%) at 91.1 155.8–157.1 (anhydrous)
PN-SYR	1:1	O5—C9 1.235(2) O4—C9 1.275(2)	O4—C9—C10 116.84 O5—C9—C10 118.93	123.59	2.671	2.6	*v*(C=O),–COOH: 1655 *v*(C–O),–COOH/ 1307 *δ*(C–H), aromatic/ 1181, 1111 v(C=N), pyridine/ 1567	132–132.5

CONCLUSION & FURTHER WORK

Crystallographic parameters of both synthesized compounds correlate to the unique thermal profiles and FTIR spectral patterns, which differ from the starting materials (unprotonated pyrodoxine base and carboxylic acids).
The short bond distances and bond angles of PN-FER-hydrate and PN-SYR indicate that pyridoxinium cation and felurate anion and pyridoxinum cation and syringate anion in both structures, PN-FER-hydrate and PN-SYR, are connected by Charge-Assisted H-bonds. Therefore, these two compounds belong to molecular salts.
Further work intends to put in evidence biopharmaceutical profiles of both cocrystals.

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